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Hydrogen-bonded chains of rings in 3-*tert*-butyl-1-phenyl-7-(4-trifluoromethylbenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-spiro-1′-cyclohexane-2′,6′-dione and 3-*tert*-butyl-7-(4-methoxybenzyl)-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-spiro-1′-cyclohexane-2′,6′-dione

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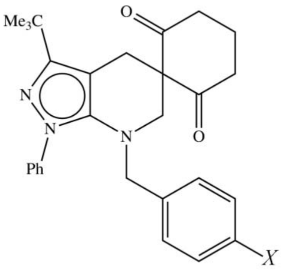
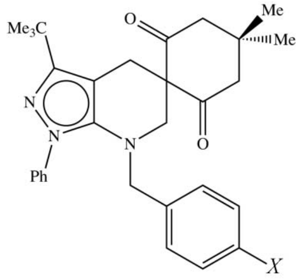
In each of 3-*tert*-butyl-1-phenyl-7-(4-trifluoromethylbenzyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-spiro-1′-cyclohexane-2′,6′-dione, $C_{29}H_{30}F_3N_3O_2$, (I), and 3-*tert*-butyl-7-(4-methoxybenzyl)-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-spiro-1′-cyclohexane-2′,6′-dione, $C_{29}H_{33}N_3O_3$, (II), the reduced pyridine ring adopts a half-chair conformation. The molecules of compound (I) are linked by two C—H···O hydrogen bonds to form a $C(5)C(5)[R^1_2(8)]$ chain of rings, while in compound (II), two C—H···O hydrogen bonds link the molecules into a $C(6)C(7)[R^2_2(11)]$ chain of rings, which is further reinforced by a C—H···π hydrogen bond. The significance of this study lies in its observation of significant differences in hydrogen-bonded structures consequent upon very minor changes in remote substituents.

Comment

In continuation of our structural study of N^7-benzyl-substituted pyrazolo[3,4-*b*]pyridine-5-spiro-1′-cyclohexane-2′,6′-diones (Cruz *et al.*, 2008; Trilleras *et al.*, 2008), itself part of a programme exploring the use of multicomponent condensation reactions, especially those induced by microwave irradiation under solvent-free conditions, for the synthesis of novel heterocycles, we now report the molecular and supramolecular structures of the two title N^7-benzyl derivatives (Figs. 1 and 2). Compounds (I) and (II) are related to the analogues (III) (Cruz *et al.*, 2008) and (IV) (Trilleras *et al.*, 2008) reported earlier, but they differ from these earlier examples in carrying no methyl substituents on the spirocyclohexane ring. Compounds (I) and (II) were synthesized using a straightforward modification of the synthetic method employed earlier (Cruz *et al.*, 2008; Trilleras *et al.*, 2008), using cyclohexane-1,3-dione in place of the 5,5-dimethylcyclohexane-1,3-dione used previously.



(I) $X = CF_3$
(II) $X = OCH_3$



(III) $X = CF_3$
(IV) $X = OCH_3$

Despite their different molecular constitutions, different space groups and different patterns of supramolecular aggregation, described below, the conformations of compounds (I) and (II) are fairly similar (Table 1). The reduced pyridine rings both adopt half-chair conformations, for which the idealized ring-puckering angles (Cremer & Pople, 1975), assuming equal bond distances throughout the rings, are $\theta = 50.8°$ and $\varphi = (60n + 30)°$, where n represents an integer. Similarly, the orientation of the three peripheral substituents relative to the heterocyclic core of the molecule is very similar in compounds (I) and (II), as shown by the relevant torsion angles. The overall molecular conformations, together with the pyramidal coordination at N7, mean that the molecules have no internal symmetry, and hence that they are chiral. However, the centrosymmetric space group in each case accommodates a racemic mixture of the two enantiomers.

The molecules of compound (I) are linked into a chain of rings by two independent C—H···O hydrogen bonds (Table 2). Atoms C6 and C53 in the molecule at (x, y, z) both act as hydrogen-bond donors to carbonyl atom O55 in the

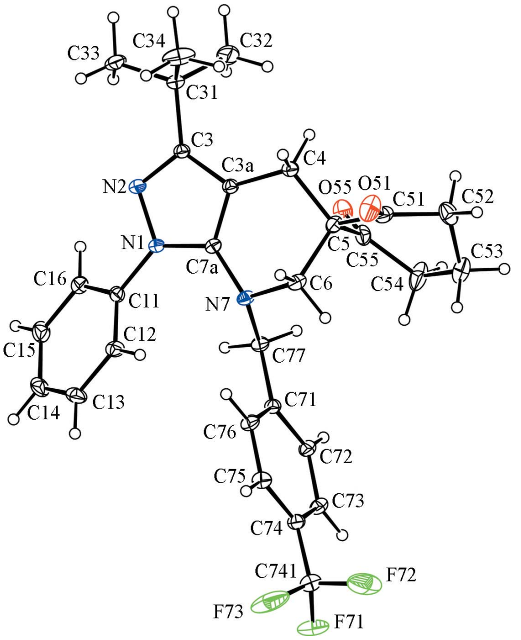


Figure 1
The molecular structure of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

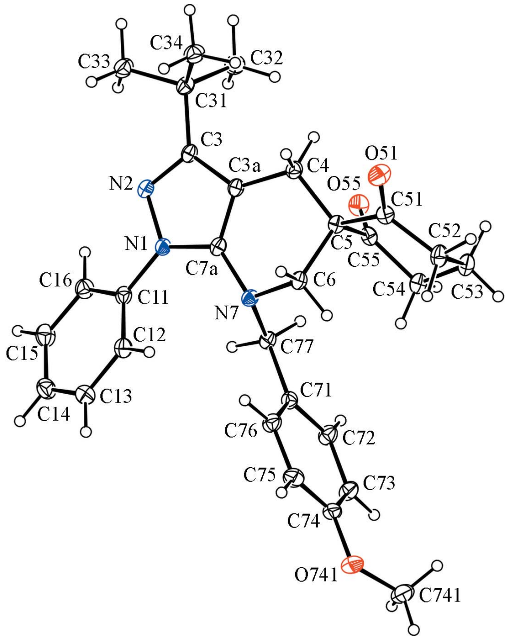


Figure 2
The molecular structure of compound (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

molecule at ($\frac{1}{2} - x$, $-\frac{1}{2} + y$, $\frac{3}{2} - z$); in this manner, molecules related by the 2_1 screw axis along ($\frac{1}{4}$, y, $\frac{3}{4}$) are linked into a $C(5)C(5)[R^1_2(8)]$ (Bernstein *et al.*, 1995) chain of rings running parallel to the [010] direction (Fig. 3). Two chains of this type, related to one another by inversion, pass through each unit cell, but there are no direction-specific interactions between adjacent chains.

In the structure of compound (II), the molecules are again linked into a chain of rings, but now three hydrogen bonds are involved (Table 2), and the chain of rings is thus more complex than that observed in the structure of compound (I). Two of the hydrogen bonds are of the C—H···O type, utilizing both of the carbonyl O atoms as acceptors, in contrast to the hydrogen bonding in compound (I); these interactions link molecules related by the 2_1 screw axis along ($\frac{1}{2}$, y, $\frac{1}{4}$) into a $C(6)C(7)[R^2_2(11)]$ chain of rings. The third hydrogen bond is of the C—H···π type, and this reinforces the chain generated by the C—H···O hydrogen bonds. As in compound (I), two inversion-related chains pass through each unit cell, but there are no direction-specific interactions between adjacent chains.

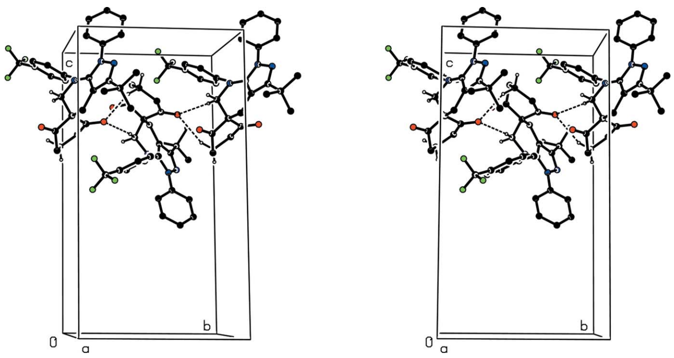


Figure 3
A stereoview of part of the crystal structure of compound (I), showing the formation of a $C(5)C(5)[R^1_2(8)]$ chain of rings along [010]. For the sake of clarity, the H atoms bonded to C atoms not involved in the motifs shown have been omitted.

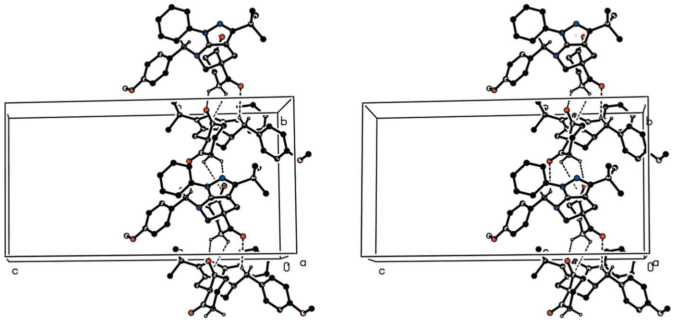


Figure 4
A stereoview of part of the crystal structure of compound (II), showing the formation of a complex chain of rings along [010]. For the sake of clarity, the H atoms bonded to C atoms not involved in the motifs shown have been omitted.

Thus, the overall molecular shapes for compounds (I) and (II) are rather similar, while their molecular constitutions vary only in the identity of the 4-substituent in the pendent benzyl ring; nonetheless, the intermolecular hydrogen bonding in compounds (I) and (II) is significantly different. It is thus interesting to note not only that these substituents, *viz.* CF_3 in (I) and OCH_3 in (II), play no direct role in the hydrogen bonding, but also that they are located well away from the atoms which do participate in hydrogen-bond formation, most of which in fact are components of the spirocyclohexane ring.

It is also of interest to compare briefly the crystal structures of compounds (I) and (II) with those of the analogous 4′,4′-

dimethyl compounds (III) (Cruz *et al.*, 2008) and (IV) (Trilleras *et al.*, 2008). Firstly, both (III) and (IV) crystallize in the triclinic system, where (III) forms an ethanol hemisolvate, while compounds (I) and (II) both form monoclinic crystals. Secondly, the heterocyclic molecules in compounds (III) and (IV) are both linked by a combination of one C—H···O hydrogen bond and one C—H···π hydrogen bond. However, the resulting structures differ not only from those of compounds (I) and (II) but also from each other. In (III), the hydrogen bonds generate a chain of edge-fused centrosymmetric rings, while in (IV) a centrosymmetric dimer is formed. Thus, the presence or absence of two peripheral methyl groups has a marked influence, albeit indirect, on the range of hydrogen bonds displayed and thence on the overall supramolecular structures.

Experimental

Microwave-induced syntheses were carried out using a focused microwave reactor (CEM Discover TM). A mixture of the appropriately substituted *N*-benzylaminopyrazole (2 mmol), cyclohexane-1,3-dione (2 mmol) and an excess of paraformaldehyde (80–100 mg) was exposed to microwave radiation at 473 K with a maximum power of 300 W for 25 min. The reaction mixtures were dissolved in hot ethanol. After cooling, the solid products were collected by filtration and washed with ethanol and then with hexane (2 × 5 ml) to afford the pure products. Colourless crystals suitable for single-crystal X-ray diffraction were grown from solutions in ethanol. For (I), yield 75%, m.p. 488–490 K; HRMS found 509.2295, $C_{29}H_{30}F_3N_3O_2$ requires 509.2290. For (II), yield 75%, m.p. 466–468 K; HRMS found 471.2524, $C_{29}H_{33}N_3O_3$ requires 471.2522.

Compound (I)

Crystal data

$C_{29}H_{30}F_3N_3O_2$
$M_r = 509.56$
Monoclinic, $P2_1/n$
$a = 11.9298$ (18) Å
$b = 10.5678$ (10) Å
$c = 19.614$ (2) Å
$\beta = 96.627$ (10)°
$V = 2456.2$ (5) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.10$ mm^{-1}
$T = 120$ (2) K
0.33 × 0.32 × 0.18 mm

Table 1
Selected geometric parameters (Å, °) for compounds (I) and (II).

Ring-puckering parameters are specified for the atom sequence N7—C6—C5—C4—C3a—C7a.

	(I)	(II)
Ring-puckering parameters		
Q	0.480 (2)	0.477 (2)
θ	51.5 (2)	49.5 (2)
φ	96.6 (4)	93.6 (3)
Torsion angles		
N2—C3—C31—C32	−119.6 (3)	−111.2 (2)
N2—C3—C31—C33	0.2 (3)	8.6 (3)
N2—C3—C31—C34	121.0 (3)	128.7 (2)
N2—N1—C11—C12	−148.4 (2)	−151.52 (19)
C6—N7—C77—C71	66.9 (3)	62.6 (2)
N7—C77—C71—C72	−157.1 (2)	−155.42 (19)
C73—C74—O74—C741		14.1 (3)

Table 2
Hydrogen bonds and short intermolecular contacts (Å, °) for compounds (I) and (II).

*Cg*1 represents the centroid of the N1/N2/C3/C3a/C7a ring.

	D—H···A	D—H	H···A	D···A	D—H···A
(I)	C6—H6A···O55^{i}	0.99	2.42	3.309 (3)	149
	C53—H53B···O55^{i}	0.99	2.54	3.448 (4)	153
(II)	C52—H52A···O55^{ii}	0.99	2.57	3.236 (3)	124
	C77—H77A···O51^{iii}	0.99	2.54	3.275 (3)	131
	C52—H52B···Cg1^{ii}	0.99	2.82	3.384 (2)	117

Symmetry codes: (i) $\frac{1}{2}-x, -\frac{1}{2}+y, \frac{3}{2}-z$; (ii) $1-x, -\frac{1}{2}+y, \frac{1}{2}-z$; (iii) $1-x, \frac{1}{2}+y, \frac{1}{2}-z$.

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{\min} = 0.975$, $T_{\max} = 0.982$
31891 measured reflections
5621 independent reflections
3742 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.055$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.061$
$wR(F^2) = 0.151$
$S = 1.07$
5621 reflections
337 parameters
H-atom parameters constrained
$\Delta\rho_{\max} = 0.43$ e Å^{-3}
$\Delta\rho_{\min} = -0.38$ e Å^{-3}

Compound (II)

Crystal data

$C_{29}H_{33}N_3O_3$
$M_r = 471.58$
Monoclinic, $P2_1/c$
$a = 9.1904$ (10) Å
$b = 11.9402$ (14) Å
$c = 22.2888$ (16) Å
$\beta = 97.287$ (9)°
$V = 2426.1$ (4) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.08$ mm^{-1}
$T = 120$ (2) K
0.39 × 0.38 × 0.16 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{\min} = 0.977$, $T_{\max} = 0.987$
37788 measured reflections
5566 independent reflections
3161 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.084$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.054$
$wR(F^2) = 0.143$
$S = 1.04$
5566 reflections
320 parameters
H-atom parameters constrained
$\Delta\rho_{\max} = 0.26$ e Å^{-3}
$\Delta\rho_{\min} = -0.32$ e Å^{-3}

For compounds (I) and (II), the space groups $P2_1/n$ and $P2_1/c$, respectively, were uniquely assigned from the systematic absences. All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H distances of 0.95 (aromatic), 0.98 (CH_3) or 0.99 Å (CH_2) and $U_{\rm iso}(H) = kU_{\rm eq}$(carrier), where $k = 1.5$ for the methyl and 1.2 for all other H atoms. The conformationally chiral reference molecules for the two compounds were chosen to have the same hand.

For both compounds, data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX*/*LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine

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structure: *OSCAIL* (McArdle, 2003) and *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PRPKAPPA* (Ferguson, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3277). Services for accessing these data are described at the back of the journal.

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